Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active cocamidopropyl betaine in the product Crop Culture Nemo Aquatic Surfactant

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This publication is available from the APVMA website: www.apvma.gov.au.

NOVEMBER 2017

CONTENTS

PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the, Department of Health, Department of Environment and Energy (DoE), and State Departments of Primary Industries.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents.

The information and technical data required by the APVMA to assess the safety of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website.

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

It indicates that the APVMA is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of the product Crop Culture Nemo Aquatic Surfactant should be granted. Submissions should relate only to matters that the APVMA is required, by legislation, to take into account in deciding whether to grant the application. These matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business 12 December 2017 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be confidential commercial information (CCI)[1] contained in submissions will be treated confidentially.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the grounds for registration should be addressed in writing to:

Case Management and Administration Unit
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604
Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

[1] A full definition of 'confidential commercial information' is contained in the Agvet Code.

Further information

Further information can be obtained via the contact details provided above.

Copies of full technical evaluation reports covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request.

Further information on public release summaries can be found on the APVMA website at www.apvma.gov.au.

1 INTRODUCTION

Crop Culture Pty Ltd has applied to the APVMA for registration of the new product Crop Culture Nemo Aquatic Surfactant containing 315 g/L cocamidopropyl betaine and in a soluble concentrate formulation.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Crop Culture Nemo Aquatic Surfactant, and approval of the new active constituent, cocamidopropyl betaine.

Crop Culture Nemo Aquatic Surfactant is to be used as a surfactant for addition to herbicide products that are approved for use in aquatic situations to control aquatic weeds. The product is expected to be used as a wetting agent to reduce the surface tension of water and enhance droplet spreadability; and as a surfactant with glyphosate to enhance weed control in aquatic situations.

The active constituent, cocamidopropyl betaine, is an active constituent approved by the APVMA. Crop Culture Nemo Aquatic Surfactant is the first product containing the active cocamidopropyl betaine proposed for the Australian market.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The active constituent, cocamidopropyl betaine, is a speciality chemical widely used as a surfactant in formulated personal care and household products such as shampoos, liquid hand soaps and dishwashing liquids.

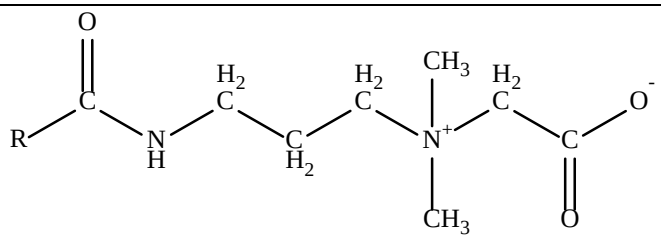
Cocamidopropyl betaine is most commonly supplied as a 30% w/w aqueous solution (a manufacturing concentrate) to a detailed manufacturer's specification; specifications for cocamidopropyl betaine are widely available in the public domain. It is derived by chemical synthesis from fatty acids of coconut oil and therefore consists of a mixture of compounds with varying hydrocarbon chain lengths corresponding to the various fatty acids present in coconut oil triglycerides.

COMMON NAME (ISO):	Cocamidopropyl betaine
CHEMICAL NAME:	{[3-(Cocamido)propyl](dimethyl)ammonio}acetate (mixture) Individual components include: {[3-(Hexanamido)propyl](dimethyl)ammonio}acetate; {[3-(Octanamido)propyl](dimethyl)ammonio}acetate; {[3-(Decanamido)propyl](dimethyl)ammonio}acetate; {[3-(Dodecanamido)propyl](dimethyl)ammonio}acetate; {[3-(Tetradecanamido)propyl](dimethyl)ammonio}acetate; {[3-(Hexadecanamido)propyl](dimethyl)ammonio}acetate; {[3-(Octadecanamido)propyl](dimethyl)ammonio}acetate; {[3-((*Z*)-Octadec-9-enamido)propyl](dimethyl)ammonio}acetate; {[3-((9*Z*,12*Z*)-Octadeca-9,12-dienamido)propyl](dimethyl)ammonio}acetate
CAS REGISTRY NUMBER:	61789-40-0

EMPIRICAL FORMULAE AND MOLECULAR WEIGHTS:

FATTY ACID COMPONENT	FORMULA	MOLECULAR WEIGHT	TYPICAL PERCENTAGE RANGE (BY MASS)[2, 3, 4]
Caproic acid	$C_{13}H_{26}N_2O_3$	258.4	0–0.8
Caprylic acid	$C_{15}H_{30}N_2O_3$	286.4	5–9
Capric acid	$C_{17}H_{34}N_2O_3$	314.5	6–10
Lauric acid	$C_{19}H_{38}N_2O_3$	342.5	44–52
Myristic acid	$C_{21}H_{42}N_2O_3$	370.6	13–19
Palmitic acid	$C_{23}H_{46}N_2O_3$	398.6	8–11
Stearic acid	$C_{25}H_{50}N_2O_3$	426.7	1–3
Oleic acid	$C_{25}H_{48}N_2O_3$	424.7	5–8
Linoleic acid	$C_{25}H_{46}N_2O_3$	422.6	0–1

[2] Being a natural product, coconut oil has a variable fatty acid composition. Fatty acid composition is typically reported on the basis of percentage by mass, often as a percentage of total fatty acids as methyl esters after derivatisation prior to GC analysis.
[3] Orsavova, J., et al, *International Journal of Molecular Science,* 2015, 16, 12871-12890
[4] Fatty Acid Composition of Some Major Oils, data from a manufacturer of processing equipment for fats and oil, Chempro (www.chempro.in/fattyacid.htm).

STRUCTURAL FORMULA:	 Where R = a hydrocarbon chain of a coconut oil fatty acid including; C_5H_{11} (caproic acid), C_7H_{15} (caprylic acid), C_9H_{19} (capric acid), $C_{11}H_{23}$ (lauric acid), $C_{13}H_{27}$ (myristic acid), $C_{15}H_{31}$ (palmitic acid), $C_{17}H_{35}$ (stearic acid), (Z)-$C_8H_{17}CH{=}CHC_7H_{14}$ (oleic acid), (9Z,12Z)-$C_5H_{11}CH{=}CHCH_2CH{=}CHC_7H_{14}$ (linoleic acid)
CHEMICAL FAMILY:	Betaines, a zwitterionic class of compounds containing both a quaternary ammonium functional group and a carboxylic acid functional group.

Physico-chemical properties of active constituent

PHYSICAL FORM:	Clear light yellow liquid
ODOUR:	Typically a slightly fatty odour
MELTING POINT:	Not applicable to the active constituent as supplied for commercial use, an aqueous manufacturing concentrate
RELATIVE DENSITY AT 20OC:	1.05 g/mL
PH:	Typically mildly acidic to neutral, ranging from 4.0–7.0
SOLUBILITY AT 20OC:	Miscible with water in all proportions
STABILITY:	Stable for up to 2 years under normal conditions

The APVMA has evaluated the chemistry aspects of cocamidopropyl betaine (manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable.

Although no impurities have been identified by the toxicological evaluation as being of greater toxicological significance than the active constituent, as cocamidopropyl betaine is a speciality chemical more commonly used in household chemical products than as an agricultural chemical, it is proposed to include specifications for a number of parameters in the Standard for the purpose of ensuring sufficient control over the quality and safety of this and future approvals.

It is proposed that the following APVMA Active Constituent Standard be established for cocamidopropyl betaine:

APVMA Active Constituent Standard for cocamidopropyl betaine manufacturing concentrate

CONSTITUENT/PARAMETER	SPECIFICATION
CHARACTERISTICS:	Clear, colourless to light yellow, mildly acidic to neutral aqueous solution, typically with a slightly fatty odour
COCAMIDOPROPYL BETAINE CONTENT:	Content must be declared, in units of g/kg or g/L. The measured content must be within the following ranges of the declared content: **Declared content** — **Tolerance** Up to 25 g/kg or g/L — ±15% Greater than 25, up to 100 g/kg or g/L — ±10% Greater than 100, up to 250 g/kg or g/L — ±6% Greater than 250 g/kg or g/L, up to 500 g/kg or g/L — ±5% Greater than 500 g/kg or g/L — ±25 g/kg or ±25 g/L Typically, cocamidopropyl betaine is supplied as a 30% w/w (300 g/kg) solution.
AMIDOAMINES (N-[(3-DIMETHYLAMINO)PROPYL]-COCONUT FATTY ACID AMIDES) CONTENT:	Maximum 15 g/kg of the cocamidopropyl betaine content
N,N-DIMETHYLPROPAN-1,3-DIAMINE (DIMETHYLAMINOPROPYLAMINE) CONTENT:	Maximum 50 mg/kg of the cocamidopropyl betaine content
SODIUM MONOCHLOROACETATE CONTENT:	Maximum 17 mg/kg of the cocamidopropyl betaine content

Other parameters which may be specified for cocamidopropyl betaine, together with typical limits (for a 30% w/w concentrate):

Total solids content: 34–36% w/w

Water content: 64–66% w/w

Sodium chloride content: 4.0–6.0% w/w

Glycerol content: maximum 3% w/w

Specific gravity: 1.04–1.08

Based on a review of the chemistry and manufacturing details provided by the applicant and of publicly available information, and noting the toxicological assessment, approval of cocamidopropyl betaine is supported.

2.2 Formulated product

The product Crop Culture Nemo Aquatic Surfactant will be formulated in Australia.

DISTINGUISHING NAME:	Crop Culture Nemo Aquatic Surfactant
FORMULATION TYPE:	Soluble concentrate (SL)
ACTIVE CONSTITUENT CONCENTRATION:	315 g/L

Physical and chemical properties of product

PHYSICAL FORM:	Clear light yellow liquid
ODOUR:	Typically a slightly fatty odour
pH VALUE:	6.0–7.5 (1% dilution)
SPECIFIC GRAVITY:	1.05
FLASH POINT:	>93.9°C
OXIDISING PROPERTIES:	Not oxidising
EXPLOSIVE PROPERTIES:	Not explosive
FLAMMABILITY:	Not flammable
CORROSIVE HAZARD:	Not corrosive
PACK SIZES:	1–1000 L
PACKAGING MATERIAL:	High density polyethylene (HDPE)
PRODUCT STABILITY:	Stable for up to 2 years when stored in the commercial packaging under normal conditions

2.3 Recommendations

Based on a review of the chemistry and manufacturing details provided by the applicant and of publicly available information, registration of Crop Culture Nemo Aquatic Surfactant is supported.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The product Crop Culture Nemo Aquatic Surfactant contains the substance cocamidopropyl betaine (315 g/L) formulated as a soluble concentrate to be mixed with other products that are approved for use in aquatic situations. This summary focuses on the toxicology of cocamidopropyl betaine with additional information on the toxicity of Crop Culture Nemo Aquatic Surfactant.

The information used to support the hazard characterization of cocamidopropyl betaine was obtained from relevant reports available in the public domain. The primary resource was the US EPA Screening Level Characterization Report for the High Production Volume Challenge Program. Secondary supporting sources include a report of the Human and Environmental Risk Assessment of household cleaning products and the Cosmetic Ingredient Review of Cocamidopropyl Betaine and related ingredients. It should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species does not necessarily indicate such effects might be observed in humans. However, from a conservative risk assessment perspective, adverse findings in animal studies are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available.

Active constituent

Chemical class

Cocamidopropyl betaine is an amphoteric surfactant. It contains both cationic (quaternary ammonium) and anionic (carboxylic acid) moieties within the structure.

Toxicokinetics and metabolism

In rats, up to 10% of an oral dose was absorbed from the intestinal tract and excreted in the urine (5–6%) and expired air (<2%). Approximately 1% remained in the carcass, and the remainder was excreted unchanged in the faeces. Tissue distribution was predominantly to those associated with urinary excretion (liver, kidney cortex, urinary bladder).

Dermal absorption

In rats, at 48 hours after dermal exposure, approximately 2–6% of the dose was absorbed. Urine was the major route of excretion with expired air and faeces being relatively minor routes. A separate study using a 10 minute exposure period, less than 0.2% was absorbed. A default value of 10% was used as a worst-case scenario in estimating exposure to the product.

Acute toxicity

Cocamidopropyl betaine is of low toxicity via the oral and dermal routes of exposure in test animals. No data are available for acute inhalation toxicity of the active constituent, it is severely irritating to the eye, irritating to the skin and there were mixed results in a variety of sensitization studies. In human volunteer studies with commercially available cocamidopropyl betaine, no evidence of sensitization was seen.

Systemic toxicity

Cocamidopropyl betaine was well tolerated in short-term and subchronic investigations, with the main target organ being the forestomach in rats. This was attributed to the irritant properties of the substance and the endpoint is not considered relevant to humans.

Genotoxicity and carcinogenicity

There was no evidence of mutagenicity or clastogenicity in a battery of genotoxicity studies *in vitro* and *in vivo*, in the presence or absence of metabolic activation.

Chronic toxicity and oncogenicity studies have not been performed via the oral route of exposure, however information was available from a chronic dermal study in mice using a hair dye formulation containing 0.09% cocamidopropyl betaine. There was no evidence of carcinogenicity in this study.

Reproductive and developmental toxicity

No specific reproductive toxicity studies are available, however histopathological investigations of the reproductive organs in the subchronic toxicity study in rats did not reveal any evidence of treatment-related effects.

In developmental toxicity studies with cocamidopropyl betaine, foetotoxicity was observed in the presence of maternal toxicity. The main observations in the dams included reduced body weight gain and food consumption, stomach ulcers and thickened stomach mucosa. Developmental effects consisted of increased resorptions, decreased number of viable foetuses and decreased foetal body weight.

Product toxicity

The formulated product, Crop Culture Nemo Aquatic Surfactant was of low acute toxicity via the oral, dermal and inhalation routes of exposure in rats. It was severely irritating to rabbit eyes, but it was neither a primary skin irritant nor a skin sensitizer.

3.2 Public health standards

Poisons scheduling

Cocamidopropyl betaine is a member of the amidopropyl betaines that are listed in Schedule 6 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). Crop Culture Nemo Aquatic Surfactant containing 315 g/L cocamidopropyl betaine is therefore included in Schedule 6.

NOEL/ADI

Acceptable Daily Intake (ADI) and Acute Reference Dose (ARfD)

The acceptable daily intake (ADI) for humans is the level of intake of an agricultural or veterinary chemical which can be ingested daily over an entire lifetime without appreciable risk to health. The acute reference dose (ARfD) is the estimate of the amount of a substance in food or drinking water, expressed on a milligram per kilogram body weight basis, that can be ingested over a short period of time, usually in one meal or during one day, without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation. The APVMA has considered the toxicological aspects of cocamidopropyl betaine, and concluded that there are no toxicological concerns to the approval of this active constituent. Furthermore, an ADI and an ARfD are deemed unnecessary and have not been established for cocamidopropyl betaine as a result of its low acute toxicity.

4 RESIDUES AND TRADE ASSESSMENT

A residues assessment was required for the use of Crop Culture Nemo Aquatic Surfactant, containing cocamidopropyl betaine, for addition to products approved for use in aquatic situations, because of the potential for exposure to crops as a result of using treated water for irrigation, and the potential for residues in animal commodities as a result of using treated water for livestock. The consumer safety and trade implications associated with the proposed use were considered.

As HBGVs were not considered necessary by the APVMA toxicology assessment, the proposed use is not expected to pose a safety concern to the consumers of crops or livestock exposed to treated water and it was not necessary to undertake a dietary risk assessment. Cocamidopropyl betaine and other approved surfactants are not currently included in the APVMA MRL standard. MRLs are not established for cocamidopropyl betaine overseas and the proposed use is not expected to pose a risk to the international trade of exposure crop or livestock commodities.

The Residues and Trade section does not have a concern with the proposed use of the new active constituent cocamidopropyl betaine as a surfactant. It is not considered necessary to establish a Table 5 entry in the MRL standard (situations where MRLs are not required) for the use of cocamidopropyl betaine as a surfactant.

5 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

5.1 Formulation, packaging, transport, storage and retailing

The product is formulated as a soluble concentrate to be mixed with other approved products. It will be applied by ground boom, handgun, knapsack and/or wiper equipment and controlled droplet applicators.

5.2 Use pattern

Crop Culture Nemo Aquatic Surfactant is intended for use as an aquatic surfactant/wetting agent for addition to products that are already approved for use in aquatic situations.

5.3 Exposure and risks during use

The product is not intended for domestic use. Operators may be exposed to the product when opening containers, when mixing and loading, during application and performing post-application or re-entry activities. The primary route of exposure will be dermal, although minor exposure via inhalation and/or ocular routes is possible.

In the absence of worker exposure data, the US EPA Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate potential worker exposure. The toxicological endpoint of concern was derived from the subchronic toxicity study in rats and in the context of this evaluation, a Margin of Exposure (MOE) in excess of 100 is considered acceptable. The MOE takes into consideration potential inter- and intra-species variability and the seriousness of the endpoint of concern.

The MOE values associated with the use of Crop Culture Nemo Aquatic Surfactant were all considered acceptable.

Acute exposure to the undiluted product is associated with the risk of eye irritation.

5.4 Exposure and risks during re-entry

Re-entry exposure is expected to be low. The product is of low acute oral, dermal and inhalational toxicity, it is non-irritating to the skin, and is not considered to be a skin sensitizer. Whereas it is a severe eye irritant, the risk of eye irritation during post application activities is considered to be negligible due to dilution.

5.5 Recommendations for safe use

Based on the human health risk assessment, the product *Crop Culture Aquatic Surfactant* is supported for use, and users should follow the First Aid Instructions and Safety Directions on the product label.

5.6 Conclusion

The registration of Crop Culture Nemo Aquatic Surfactant containing 315 g/L cocamidopropyl betaine for use with approved products in aquatic situations is supported.

6 ENVIRONMENTAL ASSESSMENT

6.1 Introduction

Crop Culture Nemo Aquatic Surfactant is an adjuvant in a soluble concentrate formulation (SL) containing 315 g/L cocamidopropyl betaine to be used in combination with herbicides for control of aquatic weeds. The product is to be added as a tank mix with glyphosate or diquat products at a maximum rate of 300 mL per 100 L (ie 94.5 g per 100 L). The tank mix is expected to be applied at a maximum spray volume of 200 L/ha which results in an application rate of 189 g/ha cocamidopropyl betaine.

The maximum approved application rates for aquatic uses of glyphosate and diquat herbicides were determined to be 3240 g/ha glyphosate (acid equivalent) and 2000 g/ha diquat. These rates have been used when considering combination toxicity with cocamidopropyl betaine applied at a rate of 189 g/ha. Because the product is applied in aquatic situations, the environmental assessment considered risks of the cocamidopropyl betaine applied by itself and in combination with glyphosate or diquat to non-target aquatic species.

6.2 Environmental fate and behaviour

Environmental fate and behaviour properties of cocamidopropyl betaine are available in publically available documents. The compound is quite water soluble and readily degraded under aerobic conditions. In various biodegradation tests, cocamidopropyl betaine was 86-100% degraded after 28 days, 90-93% degraded after 35 days and 100% after 20 days, demonstrating the product is readily biodegradable. Therefore, only acute exposure to the surfactant is considered relevant for the purpose of the aquatic safety assessment. Relevant environmental fate and behaviour properties of cocamidopropyl betaine are listed in the following table.

VAPOUR PRESSURE	<0.31 Pa (C8/C10) @ 20oC <2x10-11 Pa (C12 and greater) @ 25oC
HENRY'S LAW CONSTANT	<4×10-15 Pa m3/mol at 25°C (calculated)
SOLUBILITY IN WATER	0.0016–8.7 g/L at 25oC (calculated) ≥10 g/L at 25°C (measured)
LOG KOW	-1.28–3.63 at 25oC (calculated)
DISSOCIATION CONSTANT	Active constituent is a zwitterionic substance, which is completely dissociated in aqueous systems. At very low pH values (of about 1) active constituent is present in a protonated form
HYDROLYSIS	t1/2 > 1 year (calculated)
PHOTOCHEMICAL OXIDATIVE DEGRADATION	t1/2 6.8 to 9.0 h (calculated)
DEGRADATION IN WATER/SEDIMENT	No data
READY BIODEGRADABILITY	Readily biodegradable: 86–100% degraded after 28 days (OECD 301A/B/D/E) 90–93% degraded after 35 days (OECD 301B) 100% degraded after 20 days (Directive 84/449/EEC C.5)

6.3 Effects and associated risks to non-target species

Aquatic species could be directly exposed to cocamidopropyl betaine when it is used in combination with glyphosate or diquat immediately after application to aquatic systems for the control of aquatic weeds.

Because cocamidopropyl betaine is readily biodegradable, chronic risks were considered to be acceptable and only acute exposure was considered further.

Aquatic risks of cocamidopropyl betaine alone and in combination with glyphosate are considered to be acceptable based on information available to the APVMA.

Available information indicates that cocamidopropyl betaine is not inherently toxic to fish or amphibians. Therefore, only risks of Crop Culture Nemo Aquatic Surfactant to aquatic invertebrates and algae when mixed with diquat required further consideration. For the mixture with diquat, toxicity to aquatic invertebrates and algae were determined to be attributable to diquat alone (refer to table below). Therefore, risks of Crop Culture Nemo Aquatic Surfactant applied in combination with diquat are considered to be acceptable for approved aquatic uses of diquat.

	COCAMIDOPROPYL BETAINE	DIQUAT	COMBINATION[5] [6]
FRACTION IN COMBINATION	0.086	0.914	1.000
ACUTE TOXICITY TO AQUATIC INVERTEBRATES	EC50 1.9 mg ac/L 48h static, nominal Daphnia magna (SIAR 2006, SIDS 2007)	48h EC50 1.2 mg ac/L Daphnia magna (EC 2001)	48h EC50 1.2 mg acs/L Relative toxicity contributions: 6% + 94%
TOXICITY TO ALGAE	ErC50 1.3 mg ac/L 72h static, nominal Scenedesmus subspicatus (SIAR 2006, SIDS 2007)	72h NOEC 0.32 mg ac/L Pseudokirchneriella subcapitata (EC 2001)	NOEC 0.34 mg acs/L Relative toxicity contributions: 2% + 98%

6.4 Conclusions

The APVMA is satisfied that the proposed use of Crop Culture Nemo Aquatic Surfactant is not likely to have an unintended effect that is harmful to animals, plants or the environment if used according to the product label directions.

[5] Predicted values calculated assuming additive toxicity of active constituents in a the specified ratio (p_1:p_2) using most sensitive endpoints reported for that organism group where:

$$ECx_{CA} = \left(\frac{1}{\sum_{i-1}^{n} \frac{P_i}{ECx_i}} \right)$$

Where:
ECx_{CA} is the predicted additive toxic effect of the active constituent in combination
Pi = is the fraction of individual active constituent in the product
EC_{xi} is the effect concentration of the individual active constituent

[6] $\%_{relative\_ecotoxicity\_contribution} = \frac{\frac{p_i}{EC_{x_i}}}{\sum_{i=1}^{n} \frac{p_i}{EC_{x_i}}} \times 100$

7 EFFICACY AND SAFETY ASSESSMENT

Three trial reports were provided in support of the efficacy of Crop Culture Nemo Aquatic Surfactant (containing 315 g/L of cocoamidopropyl betaine). In two laboratory studies, Crop Culture Nemo Aquatic Surfactant was compared with a range of wetting agents in relation to its influence on surface tension and droplet spreadability. In addition, there was a field trial report that detailed the effect of several wetting agents on the performance of glyphosate in controlling grass and broadleaf weeds.

7.1 Proposed product use pattern

The proposed use of Crop Culture Nemo Aquatic Surfactant is as a surfactant for addition to products that are approved for use in aquatic situations. More details on the proposed use are provided in Section 1.

7.2 Summary of evaluation of efficacy and target safety

Efficacy

The results from the laboratory studies confirmed that Crop Culture Nemo Aquatic Surfactant reduced the surface tension of water and enhanced droplet spreadability. In the field trial, all of the glyphosate liquid treatments with Crop Culture Nemo Aquatic Surfactant at the recommended rate (200–300 mL/100 L), achieved good to excellent control of grass and broadleaf weeds. The total weed kill was equivalent to the same rates of glyphosate applied with other approved wetting agents but better than the glyphosate formulations applied without Crop Culture Nemo Aquatic Surfactant.

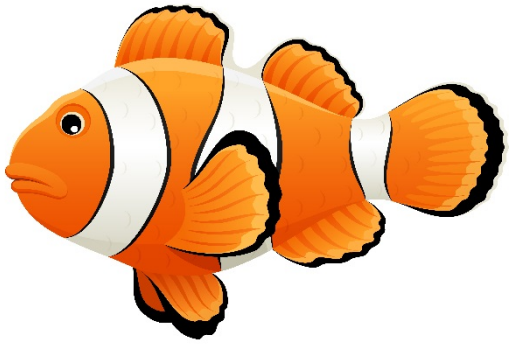
7.3 Conclusions

The evidence provided and assessed support that Crop Culture Nemo Aquatic Surfactant is effective as a surfactant and also confirms its efficacy when added to herbicides approved for use in aquatic situations, Crop Culture Nemo Aquatic Surfactant when used according to the label instructions would be effective as claimed on the label for enhancing the performance of herbicides.

8 LABELLING REQUIREMENTS

POISON

READ SAFETY DIRECTIONS BEFORE OPENING OR USING



Nemo

Aquatic Surfactant

Active constituent: 315 g/L COCAMIDAPROPYL BETAINE

Aquatic Surfactant for Addition to Products Approved for Use in Aquatic Situations

Contents: 5 L

(1 L, 10 L, 20 L, 110 L, 200 L, 1000 L)

Crop Culture Pty Ltd

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Directions for use

Situation

Nemo Aquatic Surfactant can be used for the addition to products **approved for use in aquatic situations**, (non-food crop uses only), where a surfactant/wetter is recommended, eg:

- glyphosate products—approved for use in aquatic situations
  (ie Kermit 360 Bio Herbicide, Kermit 510 Herbicide, Kermit 700 Herbicide, Roundup Biactive Herbicide by Monsanto, Nufarm Weedmaster Duo Dual Salt Technology Herbicide, Eraze 360 Bi-Aquatic Herbicide)
- diquat products—approved for use in aquatic situations
  (ie Reglone)

When mixing with the above-mentioned products, always follow the label instructions for that product.

Application Method	Rate	Critical Comments
Ground Boom	200–300 mL per 100L	Use the higher rate on waxy, hairy or hard to wet leaf surfaces.
Handgun	50–70 mL per 100L of spray solution	
Knapsack	7.5–10 mL per 15L of spray solution	
Wiper Equipment and Controlled Droplet Applicators	1.3 mL per litre of spray solution	

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION

General instructions

Nemo Aquatic Surfactant can be used for the addition to products approved for use in aquatic situations, (non-food crop uses only), where a surfactant/wetter is recommended.

Mixing

Add Nemo Aquatic Surfactant to the spray solution, which already holds the active material and the total amount of water required. Mix thoroughly. If Nemo Aquatic Surfactant is added during filling, foaming may occur.

Aquatic Areas

Do not apply this product when mixed with approved aquatic herbicides within 0.5 km up-stream of potable water intake in flowing water (ie river or stream, etc.) or within 0.5 km of a potable water intake in a standing body of water such as a lake, pond or reservoir.
Applications to moving bodies of water should be made while travelling upstream wherever possible to prevent concentration of this product in water. When making any bankside applications, do not overspray more than 0.5 m into open water. Avoid spraying across moving bodies of water, or where weeds do not exist. When emerged infestations require treatment of the total surface area of impounded water, treating the area in strips may avoid sudden impact on habitat.

Protection of wildlife, fish, crustaceans and environment

Avoid contaminating ponds, streams, rivers or waterways with the chemical or used containers. When controlling weeds in aquatic situations, refer to label directions to minimise the entry of spray into the water.

Storage and disposal

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Triple rinse the empty container before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point.
If not recycling, break, crush or puncture and deliver empty packaging for appropriate disposal to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product.

Safety directions

Will damage eyes. Avoid contact with the eyes. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and goggles. Wash hands after use.

First aid

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26. If in eyes wash out immediately with water.

Safety data sheet

For further information refer to the Safety Data Sheet (SDS), which is available from the supplier or from the manufacturer's website: www.cropculture.com.au

Conditions of sale

The use of Nemo Aquatic Surfactant being beyond the control of the manufacturer, no warranty expressed or implied is given by Crop Culture Pty Ltd regarding its suitability, fitness or efficiency for any purpose for which it is used by the buyer, whether in accordance with the directions or not and Crop Culture Pty Ltd accepts with no responsibility for any consequences whatsoever resulting from the use of this product.

APVMA Approval No.: 67157/55356

In a Transport Emergency Dial 000 Police or Fire Brigade

Batch No.:

Date of Manufacture:

ABBREVIATIONS

ac	active constituent
ACCS	Advisory Committee on Chemicals Scheduling
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ANSES	French Agency for Food, Environment and Occupational Health and Safety
ARfD	Acute Reference Dose
AUC	Area Under Curve
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft – German Federal Biological Research Centre for Agriculture and Forestry
BBCH	Biologische **B**undesanstalt, **B**undessortenamt und **CH**emische Industrie—scale used for identifying phenological stages of plants
BCF	Bio-Concentration Factor
bw	bodyweight
^{o}C	Degrees Celsius
CEC	Cation Exchange Capacity
CHO	Chinese Hamster Ovary
CIPAC	Collaborative International Pesticides Analytical Council
Codex	Codex Alimentarius Commission
Codex CXLs	Codex Maximum Residue Limits
COEX	Co-extruded (packaging material)
COEX E-VAL	COEX material using EVOH Ethylene vinyl alcohol) resin under trade name EVAL
COEX PA	COEX material using polyamide
CRD	United Kingdom Chemicals Regulation Directorate
CT	product Concentration multiplied by Time
d	day
DAA	Days After Application
DAT	Days After Treatment

DNA	Deoxyribonucleic acid
DofE	Department of Environment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC	Emulsifiable Concentrate
EC	European Commission
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EI	Export Interval
EGI	Export Grazing Interval
Eq	equivalent
ESI	Export Slaughter Interval
EUP	End Use Product
Fo	original parent generation
F_1	first generation offspring
FRAC	Fungicide Resistance Action Committee
FSANZ	Food Standards Australia and New Zealand
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GJR	Global Joint Review
GLP	Good Laboratory Practice
GPMT	Guinea Pig Maximisation Test
GVP	Good Veterinary Practice
h	hour

ha	hectare
Hb	haemoglobin
Hct	Heamatocrit
HDPE	High Density Polyethylene
HEEG	Human Exposure Expert Group
Hg	Haemoglobin
Hg	Mercury
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
HR	Highest Residue
HSIS	Hazardous Substances Information System
id	intradermal
Idf	food ingestion rate (dry weight) in grams per day
ID_{50}	dose that infects50% of the target population of organisms
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
IRM	Integrated Resistance Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
JMPR	Joint Meetings on Pesticide Residues
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
K_{ow}	Octanol-water partition coefficient
Kt	kilotonne
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms

LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOAEL	Lowest Observable Adverse Effect Level
LOD	Limit of Detection – level at which residues can be detected
LOEL	Lowest Observable Effect Level
LOQ	Limit of Quantitation – level at which residues can be quantified
mg	milligram
mL	millilitre
mN	milliNewton
MoA	Mode of Action
MoE	Margin of Exposure
mPa	milliPascal
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
ND	Not Detectable
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
Nm	nanonmetre
NOEC/NOEL	No Observable Effect Concentration Level
NOER	No Observable Effect Rate
OC	Organic Carbon
OD	Oil Dispersion (oil-based suspension concentrate)
OECD	Organisation of Economic Cooperation and Development
OGTR	Office of the Gene Technology Regulator
OM	Organic Matter

Pa	Pascals
PCV	Pack Cell Volume
PE	PolyEthylene
PEC	Predicted Environmental Concentration
PE/EVOH	Polyethylene with ethylene vinyl alcohol
PET	Polyethylene terephthalate
PHI	Post-Harvest Interval
pKa	Dissociation constant (acid)
PMRA	Pest Management regulatory Agency (Canada)
PNEC	Predicted No Effect Concentration
po	oral
PP	PolyPropylene
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
RCP	Restricted Chemical Product
RNA	Ribonucleic acid
s	second
sc	subcutaneous
SC	Suspension Concentrate
SCBA	Self-Contained Breathing Apparatus
SE	SuspoEmulsion
SG	Soluble granule
STMR	Supervised Trials Median Residue
STMR-P	STMR corrected for processing

SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
SWA	Safe Work Australia
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T_{max}	Time to achieve maximum concentration
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
$T_{1/2}$	Elimination half-life
UDS	Unscheduled DNA Synthesis
µg	microgram
US EPA	United States Environmental Protection Agency
UV	Ultra Violet light
vmd	volume median diameter
WBC	White Blood Count
WG	Water Dispersible Granule
WHP	Withholding Period
w/v	Weight/volume

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	repels water
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Total Radioactive Residue (TRR)	The total amount of ^{14}C-labelled active constituent and its metabolites detected in residue studies
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

REFERENCES

US EPA (1998). United States Environmental Protection Agency (US EPA). *The Pesticide Handlers Exposure Database (PHED), version 1.1-PHED Surrogate Exposure Guide, Estimates of Worker Exposure.* US EPA, Washington DC, United States, 1998.